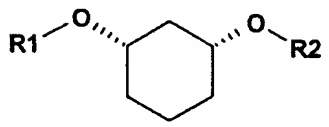
We claim:

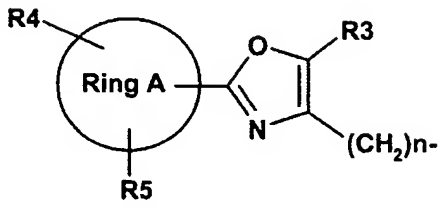
1. A process for preparing a chiral, nonracemic compound of the formula I



(I)

wherein:

R^1 is



wherein:

ring A is phenyl, an 8-, 9-, 10-, 11-, 12-, 13-, or 14-membered aromatic ring, $(C_3$-$C_8)$-cycloalkyl or a 5-, 6-, 7-, 8-, 9-, 10-, 11- or 12-membered heteroaromatic ring optionally containing one to four heteroatoms selected from the group of N, O and S;

R^3 is H, F, Cl, Br, OH, NO_2, CF_3, OCF_3, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_8)$-cycloalkyl or phenyl;

R^4, R^5 are each independently H, F, Cl, Br, OH, NO_2, CF_3, OCF_3, OCF_2H, OCF_2-CF_3, OCF_2-CHF_2, SCF_3, O-phenyl, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl or O-$(C_1$-$C_6)$-alkyl-O-$(C_1$-$C_3)$-alkyl;

n is 1, 2 or 3; and

R^2 is $(C_1$-$C_8)$-alkyl wherein one or more CH_2 groups in said $(C_1$-$C_8)$-alkyl group is optionally replaced by O, CO, S, SO or SO_2, and said $(C_1$-$C_8)$-alkyl group is optionally mono-, di-, or trisubstituted by F, Cl, Br, CF_3, CN, NO_2, NHAc, NHBoc, NH-CO-$C(CH_3)_3$, hydroxyl,

OCF_3, O-(C_1-C_6)-alkyl, COOH, CO-benzoxy, CO-O(C_1-C_6)-alkyl, tetrazole, thiazolidin-2,4-dione, indole or (C_6-C_{10})-aryl,

wherein said thiazolidin-2,4-dione and aryl groups are optionally substituted by F, Cl, Br, CF_3, CN, NO_2, NHAc, NHTs, NHBoc, NHCbz, NH-CO-$C(CH_3)_3$, hydroxyl, OCF_3, O-(C_1-C_6)-alkyl, COOH, CO-benzoxy, CO-O(C_1-C_6)-alkyl, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl or tetrazole, or

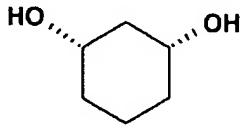
R^2 is an OH protecting group (PG) selected from the group comprising benzyloxymethyl, benzyl, para-methoxybenzyl or tert-butyldimethylsilyl;

which comprises:

A)

a) <u>alkylation (alk-R2/alk-PG)</u>

reacting cis-1,3-cyclohexanediol of the formula (II)



(II)

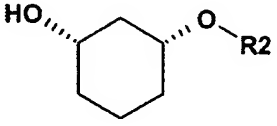
with a compound of the formula (III)

$$X^1\text{-}R^2 \qquad \text{(III)}$$

where R^2 is as defined above and

X^1 is Cl, Br, I, OMs, OTs, OTf;

in the presence of bases in a suitable solvent to give a racemic compound of the formula (IV)

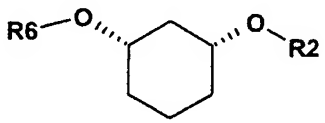


(IV)

where R^2 is as defined above;

b1) <u>enzymatic ester formation (EF) + separation (S)</u>

subjecting the resulting compounds of the formula (IV) to stereoselective enzymatic ester formation (EF), in which the alcohols are admixed with an acyl donor and the enzyme in an organic solvent and the resulting mixture is stirred at -20 to 80°C and, after the reaction has ended, one stereoisomer is present as an ester of the formula (V)



(V)

wherein

R^6 is C(=O)-(C_1-C_{16})-alkyl, C(=O)-(C_2-C_{16})-alkenyl, C(=O)-(C_3-C_{16})-alkynyl, C(=O)-(C_3-C_{16})-cycloalkyl,

wherein one or more carbon atoms in said C(=O)-(C_1-C_{16})-alkyl, C(=O)-(C_2-C_{16})-alkenyl, C(=O)-(C_3-C_{16})-alkynyl and C(=O)-(C_3-C_{16})-cycloalkyl groups are optionally replaced by oxygen atoms, and wherein said C(=O)-(C_1-C_{16})-alkyl, C(=O)-(C_2-C_{16})-alkenyl, C(=O)-(C_3-C_{16})-alkynyl and C(=O)-(C_3-C_{16})-cycloalkyl groups are optionally substituted by 1, 2 or 3 substituents selected from the group of F, Cl, Br, CF_3, CN, NO_2, hydroxyl, methoxy, ethoxy, phenyl and CO-O(C_1-C_4)-alkyl or CO-O(C_2-C_4)-alkenyl,

wherein said CO-O(C_1-C_4)-alkyl and CO-O(C_2-C_4)-alkenyl substituents are optionally substituted by 1, 2 or 3 substituents selected from the group of F, Cl, Br or CF_3, and

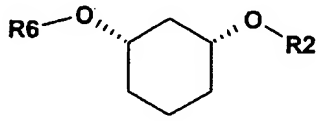
R^2 is as defined above,

and the other stereoisomer is present unchanged as the alcohol of the formula (IV), and are therefore separated from each other by utilizing their different chemical or physicochemical properties (separation S)

or

b2) enzymatic ester hydrolysis [=chemical esterification (CE) + enzymatic hydrolysis (EH)] + separation (S)

subjecting the resulting compound of the formula (IV) to a stereoselective enzymatic ester hydrolysis, in which the racemic alcohol is initially converted by chemical esterification (CE), for example by means of acid chloride R^6-Cl or acid anhydride R^6-O- R^6, in the presence of bases, to the racemic ester of the formula (V)



(V)

wherein R^6 and R^2 are each as defined above,

which, to carry out the stereoselective enzymatic ester hydrolysis (EH), is then taken up in homogeneous or heterogeneous, aqueous, aqueous-organic or organic medium, and reacted, in the presence of an enzyme in the case of hydrolysis with water and in the case of alcoholysis with an alcohol, at a temperature of 10-80°C, and after the reaction has ended, one stereoisomer is present as the alcohol of the formula (IV) and the other is present unchanged as the ester of the formula (V) and can thus be separated from each other as described under b1), and

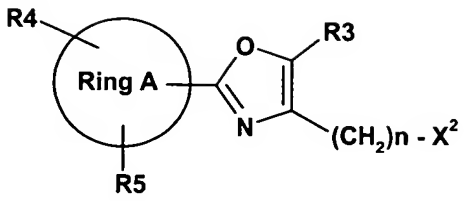
the enantiomer of the formula (IV) occurring as an alcohol is further processed as described under d), or

c) chemical hydrolysis (CH)

hydrolyzing the enantiomer of the formula (V) occurring as an ester to the chemically enantiomeric alcohol by known methods and

d) alkylation (alk- R^1)

reacting further with a compound of the formula (VI)



(VI)

wherein

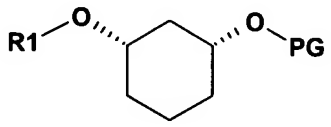
ring A, R^3, R^4, R^5 and n are each as defined above and

X^2 is Cl, Br, I, OTs, Oms or OTf;

in the presence of bases in a suitable solvent to give the compound of the formula (I), and

e) <u>detachment of the protecting group PG (detPG)</u>

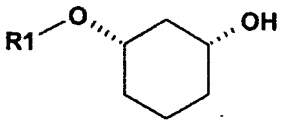
if R^2 is an OH protecting group (PG) as defined above under R^2, converting the compound of the formula (Ia)



(Ia)

wherein R^1 and PG are each as defined above,

by detaching the protecting group by known methods to a compound of the formula (VII)



(VII)

wherein R^1 is as defined above,

f) <u>alkylation (alk- R^2)</u>

then reacting it with a compound of the formula (III)

X^1-R^2 (III)

wherein X^1 and R^2 are each as defined above,

in the presence of bases in a suitable solvent to give a compound of the formula (I), the product or the enantiomeric form,

it being also possible to change the sequence of individual reaction steps as described above under A):

A) alk-R^2 → EF + S/CE + EH + S [→ CH] → alk- R^1 [→ DetPG → alk- R^2] → product/enantiomeric form

to:

B) alk- R^1 → EF + S/CE + EH + S [→ CH] → alk- R^2 [→ DetPG → alk- R^2] → product/enantiomeric form

or

C) alk-PG → EF + S/CE + EH + S → CH → alk- R^2 → DetPG → alk- R^1 → product/enantiomeric form

or

D) alk-PG → EF + S/CE + EH + S → alk- R^1 → DetPG → alk- R^2 → product/enantiomeric form.

2. The process of Claim 1, wherein the processes C) and D) are employed.

3. The process of Claim 2, wherein compounds of the formula (III)

$X^1 - R^2$ (III)

are used wherein

X^1 is Cl, Br, I, OMs or OTs.

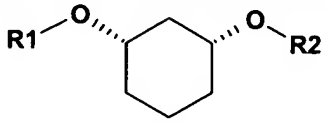
4. The process of Claim 3, wherein compounds of the formula (III)

$$X^1 - R^2 \quad (III)$$

are used wherein

X^1 is Cl, Br or I.

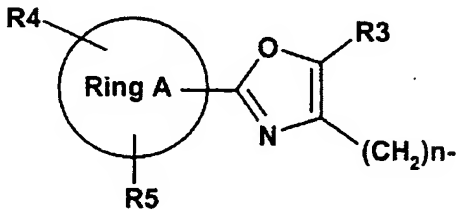
5. The process of Claim 4, wherein a compound of the formula (I)



(I)

is prepared where:

R^1 is



wherein

ring A is phenyl, (C_3-C_8)-cycloalkyl, a fused/bicyclic 8-, 9-, 10-, 11-, 12-, 13- or 14-membered aromatic ring, or a 5-, 6-, 7-, 8-, 9-, 10-, 11- or 12-membered heteroaromatic ring optionally containing one or more heteroatoms selected from the group of N, O and S;

R^3 is H, CF_3, (C_1-C_6)-alkyl, (C_3-C_8)-cycloalkyl or phenyl;

R^4, R^5 are each independently H, F, Br, CF_3, OCF_3, (C_1-C_6)-alkyl or O-(C_1-C_6)-alkyl;

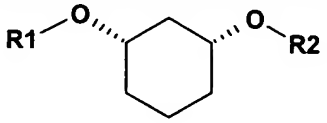
n is 1 or 2; and

R^2 is (C_1-C_8)-alkyl wherein one or more CH_2 groups in the said (C_1-C_8)-alkyl group is optionally replaced by O, CO, S, SO or SO_2,

and said (C_1-C_8)-alkyl group is optionally mono-, di- or trisubstituted by F, Cl, Br, CF_3, CN, NO_2, NHAc, NHBoc, NH-CO-$C(CH_3)_3$, hydroxyl, OCF_3, O-(C_1-C_6)-alkyl, COOH, CO-benzoxy, CO-O(C_1-C_6)-alkyl, tetrazole, thiazolidin-2,4-dione, indole or (C_6-C_{10})-aryl,

wherein said thiazolidin-2,4-dione and (C_6-C_{10})-aryl substituents are optionally substituted by F, Cl, Br, CF_3, CN, NO_2, NHAc, NHTs, NHBoc, NHCbz, NH-CO-$C(CH_3)_3$, hydroxyl, OCF_3, O-(C_1-C_6)-alkyl, COOH, CO-benzoxy, CO-O(C_1-C_6)-alkyl, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl or tetrazole.

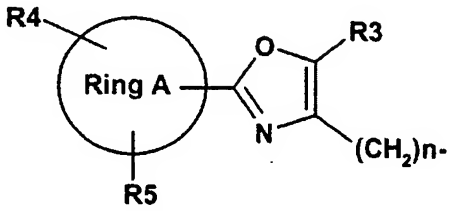
6. The process of Claim 5, wherein a compound of the formula (I)



(I)

is prepared wherein:

R^1 is



wherein

ring A is phenyl;

R^3 is (C_1-C_4)-alkyl;

R^4, R^5 are each independently H, (C_1-C_4)-alkyl or O-(C_1-C_4)-alkyl;

n is 1; and

R^2 is (C_1-C_8)-alkyl wherein one or more CH_2 groups in said (C_1-C_8)-alkyl group are optionally replaced by O, CO, S, SO or SO_2, and

wherein said (C_1-C_8)-alkyl group is optionally mono-, di-, or trisubstituted by F, Cl, Br, CF_3, CN, NO_2, NHAc, NHBoc, NH-CO-$C(CH_3)_3$, hydroxyl, OCF_3, O-(C_1-C_6)-alkyl, COOH, CO-benzoxy, CO-O(C_1-C_6)-alkyl, tetrazole, thiazolidin-2,4-dione, indole or (C_6-C_{10})-aryl,

wherein said thiazolidin-2,4-dione and (C_6-C_{10})-aryl substituents are optionally substituted by F, Cl, Br, CF_3, CN, NO_2, NHAc, NHTs, NHBoc, NHCbz, NH-CO-$C(CH_3)_3$, hydroxyl, OCF_3, O-(C_1-C_6)-alkyl, COOH, CO-benzoxy, CO-O(C_1-C_6)-alkyl, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl or tetrazole.